



**Manchester
Metropolitan
University**

Britten, Thomas Kenton and McLaughlin, Mark Gerard ORCID logoORCID:
<https://orcid.org/0000-0002-5999-4703> (2020) Brønsted Acid Catalyzed Peterson Olefinations. The Journal of Organic Chemistry, 85 (2). pp. 301-305. ISSN 0022-3263

Downloaded from: <https://e-space.mmu.ac.uk/624491/>

Version: Accepted Version

Publisher: American Chemical Society (ACS)

DOI: <https://doi.org/10.1021/acs.joc.9b02489>

Please cite the published version

<https://e-space.mmu.ac.uk>

Featured Article

Brønsted Acid Catalyzed Peterson Olefinations

Thomas Kenton Britten, and Mark Gerard McLaughlin

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.9b02489 • Publication Date (Web): 27 Nov 2019

Downloaded from pubs.acs.org on November 30, 2019

Just Accepted

"Just Accepted" manuscripts have been peer-reviewed and accepted for publication. They are posted online prior to technical editing, formatting for publication and author proofing. The American Chemical Society provides "Just Accepted" as a service to the research community to expedite the dissemination of scientific material as soon as possible after acceptance. "Just Accepted" manuscripts appear in full in PDF format accompanied by an HTML abstract. "Just Accepted" manuscripts have been fully peer reviewed, but should not be considered the official version of record. They are citable by the Digital Object Identifier (DOI®). "Just Accepted" is an optional service offered to authors. Therefore, the "Just Accepted" Web site may not include all articles that will be published in the journal. After a manuscript is technically edited and formatted, it will be removed from the "Just Accepted" Web site and published as an ASAP article. Note that technical editing may introduce minor changes to the manuscript text and/or graphics which could affect content, and all legal disclaimers and ethical guidelines that apply to the journal pertain. ACS cannot be held responsible for errors or consequences arising from the use of information contained in these "Just Accepted" manuscripts.

Brønsted Acid Catalyzed Peterson Olefinations.

Thomas K. Britten and Mark G. McLaughlin*

Department of Natural Sciences, Manchester Metropolitan University, Chester Street, Manchester, United Kingdom, M15GD.

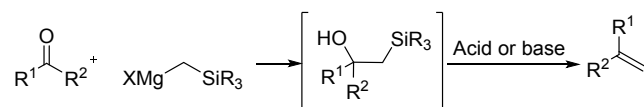
Supporting Information Placeholder

ABSTRACT: A mild and facile Peterson olefination has been developed employing low catalyst loading of the Brønsted acid HNTf₂. The reactions are typically performed at room temperature, with the reaction tolerant to a range of useful functionalities. Furthermore, we have extended this methodology to the synthesis of enynes.

Introduction

The Peterson olefination has enjoyed sustained interest from the synthetic community since its discovery in the late 1960's (Scheme 1).¹ This is unsurprising, given the large numbers of bioactive natural products that contain alkene functional groups.² In its simplest guise, the Peterson olefination, or silyl-Wittig, is the elimination of β-silyl alcohols, promoted by the β-silicon effect.³

Scheme 1. General Peterson Olefination



One key characteristic of the Peterson is that it can afford both *E* and *Z* isomers depending on the conditions employed.⁴ Routinely employing super-stoichiometric quantities of strong acids or bases results in a facile elimination reaction, however due to the necessity of large quantities of reagents, functional group tolerance and utility in complex target synthesis remains an issue. Recent advances in rendering the Peterson olefination catalytic have resulted in a small number of strategies (Scheme 2),⁵ however this area remains underexplored.

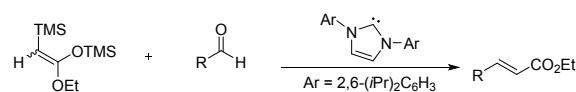
Brønsted acid catalysts have become a mainstay of modern synthetic chemistry, and have been successfully used in a wide range of applications.⁶ BINOL-derived phosphoric acids and amides have shown great utility in the synthesis of complex scaffolds via numerous transformations,⁷ as have urea⁸ and thiourea derivatives.⁹ These Brønsted acids have been shown to activate carbonyls, imines as well as olefins to form the corresponding salts or carbocations.¹⁰ Furthermore, Brønsted acids have been shown to activate hydroxyl groups, but typically require much higher catalyst loadings.¹¹

A potential solution is to use more acidic Brønsted acids, such as the readily available triflic acid, TfOH.¹² Although useful, its toxicity and difficulty in handling renders its use problematic. Nevertheless, the synthetic utility of super Brønsted acids has

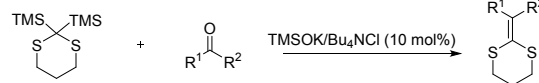
resulted in several alternatives being reported. Of these, triflimide HNTf₂, has shown promise.¹³ Not only is it easier to handle (solid vs viscous oil) but it's pK_a is a fold lower than TfOH (-12.3 vs -11.4 in DCE),¹⁴ allowing for potentially milder activation conditions. We therefore envisaged that we could take advantage of this increased acidity, and develop a general catalytic Peterson olefination employing low catalyst loading.

Scheme 2. Previously Reported Catalytic Peterson's

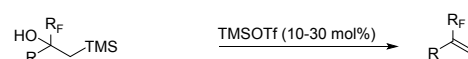
He (2016)



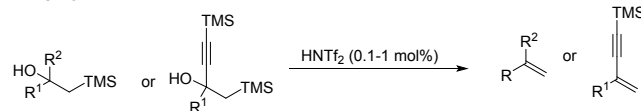
O'Shea (2015)



Leadbetter (2014)

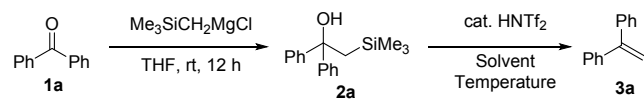


This work



Results and Discussion

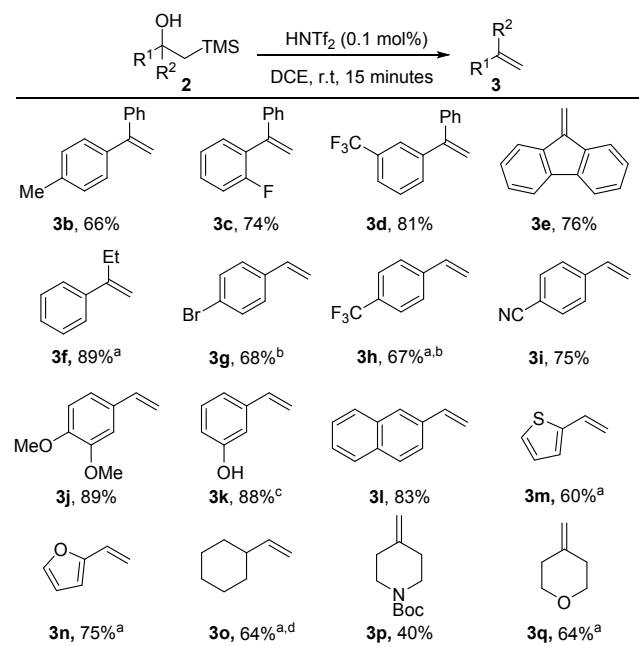
We began our investigation using crude **2a**, readily formed by the addition of TMSCH₂MgCl to benzophenone (**1a**) followed by simple DCM workup, and 10 mol% HNTf₂ in refluxing DCM. To our delight, the reaction was complete within 15 minutes, affording the 1,1-disubstituted alkene in 90% yield. Reducing the catalyst loading to 1 mol% had little effect on the reaction, nor did running the reaction at room temperature. Further reducing the catalyst loading to 0.1 mol% produced **3a** in 89% yield after 15 minutes. Further attempts to increase the yield through varying the solvent were unsuccessful (Table 1). We also performed the reaction on 5.5 mmol scale, which resulted in effectively the same yield as the small scale reaction.

Table 1. Optimization Studies


Entry	Cat. loading (mol %)	Solvent	Temp (°C)	Yield (%) ^a
1	10	DCM	40	90
2	1	DCM	40	87
3	1	DCM	rt	85
4	0.1	DCM	rt	88
5	0.1	1,2-DCE	rt	89 (88) ^b
6	0.1	MeCN	rt	88
7	0.1	Acetone	rt	60
8	-	1,2-DCE	rt	n.r

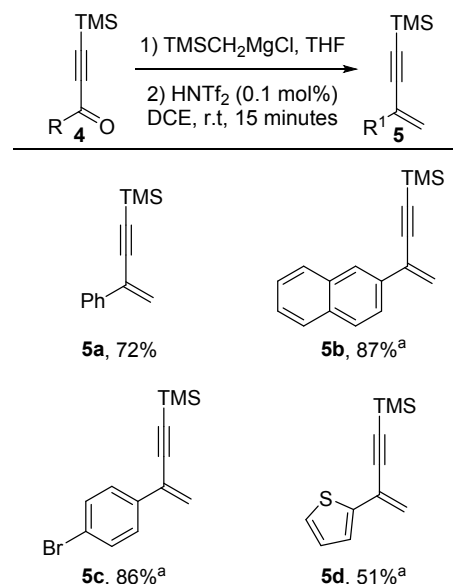
^a Isolated Yields, ^b 5.5 mmol scale (starting from 1.0 g of **1a**)

With these conditions in hand, we probed the functional group tolerance of the reaction. We initially focused on the use of aldehydes and ketones to provide the corresponding styrenes. As shown, the reaction is tolerant to a range of both aromatic and alkyl substituents, providing the desired olefins in good yield after 15 minutes. Benzophenone derived products all reacted well (**3a-3d**), as did fluorenone (**3e**) and propionphenone (**3f**). Products derived from aldehydes were also synthesized via this methodology, with electron withdrawing groups such as bromide (**3g**) trifluoromethyl (**3h**) and cyano (**3i**) providing the styrene in good yields. Electron donating groups also proved successful, giving the desired products (**3j-3l**) efficiently and in good yields. Heterocyclic groups are also well tolerated, with the corresponding thiophene and furan (**3m** and **3n**) derivatives being produced. Finally, this methodology can extend to cyclic alkyl (**3o**) and heteroalkyl (**3p** and **3q**) groups, providing the desired olefins in synthetically useful yields. Of particular note is the compatibility with carbamate protecting groups, which are well known to cause issues in traditional Peterson olefinations.

Scheme 3. Substrate Scope

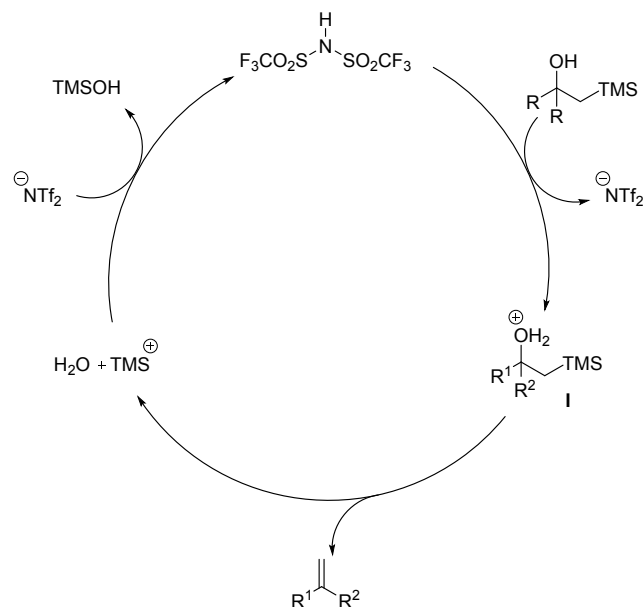
^a Reaction performed in CDCl₃ and the yield was determined through ¹H NMR spectroscopy of the reaction mixture using 1,3,5-trimethoxybenzene as an internal standard; ^b 1 mol% HNTf₂ used; ^c Reaction performed in MeCN; ^d 0.5 mol% HNTf₂ used

We then turned our attention to the use of readily available propargylic ketones to provide enynes following the Peterson olefination. As shown, the reaction proceeded smoothly, affording the desired enyne products in moderate to high yields (Scheme 4). This is one of very few examples of using the Peterson to produce these high value compounds,¹⁵ and is, to the best of our knowledge, the only catalytic version of the Peterson to achieve this.

Scheme 4. Synthesis of Enynes

^a Reaction performed in CDCl₃ and the yield was determined through ¹H NMR spectroscopy of the reaction mixture using 1,3,5-trimethoxybenzene as an internal standard

A proposed mechanism is shown below (Figure 1). Owing to the pK_a differential between the catalyst and the alcohol, we envisage that a facile deprotonation event occurs. This results in intermediate **I**, which then undergoes elimination to form the desired product. The silylenium cation¹⁶ is then trapped out with water to produce silanol, and the resultant proton generated via this process regenerates the catalyst.

Figure 1. Proposed Catalytic Cycle

In summary, we have developed a highly efficient, one pot catalytic Peterson olefination employing 0.1 mol% bistriflimide as catalyst. As shown, the reaction is tolerant of a range of functional groups, including groups unsuited to the traditional Peterson reaction (**3i**, **3k** and **3p**). We have also investigated the use of propargylic ketones in the reaction, affording a small library of enynes. Investigations towards its applicability in complex natural product synthesis is currently underway.

EXPERIMENTAL SECTION

Solvents and reagents

All solvents were purchased from commercial sources and used without purification (HPLC or analytical grade). Anhydrous solvent was obtained from a Pure Solv™ Solvent Purification System. Standard vacuum line techniques were used and glassware was oven dried prior to use. Organic solvents were dried during workup using anhydrous Na₂SO₄. All calcium catalyzed reactions were done without the need for anhydrous or air free conditions.

Purification and chromatography

Thin Layer Chromatography (TLC) was carried out using aluminum plates coated with 60 F254 silica gel. Plates were visualized using UV light (254 or 365 nm) or staining with 1% aq. KMnO₄. Normal-phase silica gel chromatography was carried out using either a Biotage Isolera One flash column chromatography system (LPLC) or traditional flash column chromatography using Geduran® Silica gel 60, 40–63 microns RE.

Characterization

Infrared spectroscopy was carried out with a Nicolet® 380 FT/IR – Fourier Transform Infrared Spectrometer. Only the most significant frequencies have been considered during the characterization and selected absorption maxima (ν_{max}) recorded in wavenumbers (cm⁻¹). NMR spectra were recorded using a JEOL® ECS-400 MHz spectrometer using the deuterated solvent stated. Chemical shifts (δ) quoted in parts per million (ppm) and referenced to the residual solvent peak. Multiplicities are denoted as s- singlet, d- doublet, t- triplet, q- quartet and quin- quintet and derivatives thereof (br denotes a broad resonance peak). Coupling constants recorded as Hz and round to the nearest 0.1 Hz. High Resolution Mass Spectrometry (HRMS) was recorded using an Agilent Technologies® 6540 Ultra-High-Definition (UHD) AccurateMass equipped with a time of flight (Q-TOF) analyzer and the samples were ionized by ESI techniques and introduced through a high pressure oil chromatography (HPLC) model Agilent Technologies® 1260 Infinity Quaternary LC system.

Propargyl ketones **4a-d** were synthesized according to previously published procedures.¹⁷

General Procedure A: Synthesis of Alkenes. (Trimethylsilylmethyl)magnesium chloride (1.3 M solution in THF, 3.0 equiv.) was added dropwise to a stirred solution of aldehyde/ketone (1.0 equiv.) in THF (0.2 M) at 0 °C under argon and then stirred at room temperature overnight. The reaction mixture was cooled to 0 °C and quenched with a saturated aqueous solution of NH₄Cl (5 mL). The aqueous phase was extracted with CH₂Cl₂ (3 x 5 mL), dried (Na₂SO₄) and evaporated under reduced pressure to give the crude product, which was used without further purification. A stock solution of HNTf₂ in 1,2-DCE (0.01 M, 0.1–1.0 mol%) was added in one portion to a stirred solution of the crude product in 1,2-DCE (0.5 M) at room temperature, then stirred for 15 minutes. The solvent was removed under reduced pressure and the crude product was purified by flash column chromatography using an appropriate solvent system, as described for each individual procedure. *Note: stock solutions of trifluoromethanesulfonimide in 1,2-DCE were stored in the fridge to avoid decomposition.*

General Procedure B: NMR Reactions in the Synthesis of Alkenes. A stock solution of trifluoromethanesulfonimide in 1,2-

DCE (0.01 M, 0.1–1.0 mol%) was added in one portion to a stirred solution of the crude product in CDCl₃ (0.5 M) at room temperature, then stirred for 15 minutes. An aliquot of the reaction mixture was removed (0.6 mL, 0.3 mmol of substrate), combined with 1,3,5-trimethoxybenzene and analyzed by ¹H NMR spectroscopy. The amount of alkene present was quantified using the following equation: $n_A = n_{IS} \times r_{A/IS}$, where n_A = mmol of analyte, n_{IS} = mmol of internal standard and $r_{A/IS}$ = ratio of analyte to internal standard (see supporting information for example calculation).

1,1'-(ethene-1,1-diyl)dibenzene (3a). Using general procedure A, benzophenone (182 mg, 1.00 mmol) and HNTf₂ (0.1 mL, 0.1 mol%) provided alkene **3a** (161 mg, 0.89 mmol, 89%) as a colorless oil after purification by flash column chromatography (eluent: hexane).

R_f (hexane) = 0.38

¹H NMR (400 MHz, CDCl₃); δ 7.36–7.32 (m, 5H), 5.47 (s, 1H).

¹³C{¹H} NMR (100 MHz, CDCl₃); δ 150.2, 141.6, 128.4, 128.3, 127.9, 114.5.

Spectral data in accordance to previously published data.¹⁸

1-Methyl-4-(1-phenylethenyl)benzene (3b). Using general procedure A, 4-methylbenzophenone (196 mg, 1.00 mmol) and HNTf₂ (0.1 mL, 0.1 mol%) provided alkene **3b** (133 mg, 0.68 mmol, 68%) as a colorless oil after purification by flash column chromatography (eluent: hexane).

R_f (hexane-EtOAc, 7:1) = 0.59

¹H NMR (400 MHz, CDCl₃); δ 7.36–7.31 (m, 5H), 7.25 (d, J = 8.1 Hz, 2H), 7.15 (d, J = 8.1 Hz, 2H), 5.44 (d, J = 1.2 Hz, 1H), 5.42 (d, J = 1.2 Hz, 1H), 2.38 (s, 3H).

¹³C{¹H} NMR (100 MHz, CDCl₃); δ 150.0, 141.8, 138.7, 137.7, 129.0, 128.4, 128.29, 128.26, 127.8, 21.3.

Spectral data in accordance to previously published data.¹⁹

1-Fluoro-2-(1-phenylethenyl)benzene (3c). Using general procedure A, 2-fluorobenzophenone (168 μL, 1.00 mmol) and HNTf₂ (0.1 mL, 0.1 mol%) provided alkene **3c** (147 mg, 0.74 mmol, 74%) as a colorless oil after purification by flash column chromatography (eluent: hexane).

R_f (hexane) = 0.26

¹H NMR (400 MHz, CDCl₃); δ 7.36–7.27 (m, 7H), 7.17–7.05 (m, 2H), 5.76 (d, J = 1.1 Hz, 1H), 5.43 (s, 1H).

¹³C{¹H} NMR (100 MHz, CDCl₃); δ 160.3 (d, J_F = 248.5 Hz), 144.3, 140.7, 131.7 (d, J_F = 3.4 Hz), 129.5 (d, J_F = 7.9 Hz), 129.3, 128.4, 127.9, 126.9, 124.1 (d, J_F = 3.6 Hz), 117.2 (d, J_F = 1.7 Hz), 115.9 (d, J_F = 22.2 Hz).

¹⁹F (376 MHz, CDCl₃) δ -113.1

Spectral data in accordance to previously published data.²⁰

1-(1-Phenylethenyl)-3-(trifluoromethyl)benzene (3d). Using general procedure A, 3-(trifluoromethyl)benzophenone (249 mg, 1.00 mmol) and HNTf₂ (0.1 mL, 0.1 mol%) provided alkene **3d** (199 mg, 0.80 mmol, 81%) as a colorless oil after purification by flash column chromatography (eluent: hexane).

R_f (hexane) = 0.29

¹H NMR (400 MHz, CDCl₃); δ 7.62–7.43 (m, 4H), 7.38–7.30 (m, 5H), 5.55 (d, J = 0.6 Hz, 1H), 5.50 (d, J = 0.6 Hz, 1H).

¹³C{¹H} NMR (100 MHz, CDCl₃); δ 149.0, 142.4, 140.7, 131.7, 130.8 (q, J_F = 31.9 Hz), 128.8, 128.5, 128.3, 125.6, 125.1 (q, J_F = 3.5 Hz), 124.6 (q, J_F = 3.6 Hz), 122.9, 115.8.

¹⁹F (376 MHz, CDCl₃) δ -62.5

Spectral data in accordance to previously published data.²¹

9-Methylidene-9H-fluorene (**3e**). Using general procedure A, 9-fluorenone (181 mg, 1.00 mmol) and HNTf₂ (0.1 mL, 0.1 mol%) provided alkene **3e** (135 mg, 0.76 mmol, 76%) as a white solid after purification by flash column chromatography (eluent: hexane).

R_f (hexane) = 0.33

¹H NMR (400 MHz, CDCl₃); δ 7.76–7.10 (m, 4H), 7.41–7.30 (m, 4H), 6.09 (s, 2H).

¹³C{¹H} NMR (100 MHz, CDCl₃); δ 143.5, 140.3, 138.2, 128.9, 127.2, 121.1, 119.9, 108.0.

Spectral data in accordance to previously published data.²⁰

(*But-1-en-2-yl*)benzene (**3f**). Using general procedure B, propiophenone (130 μL, 0.98 mmol), HNTf₂ (0.1 mL, 0.1 mol%) and 1,3,5-trimethoxybenzene (3.0 mg, 0.018 mmol) provided alkene **3f** (89% NMR yield).

1-Bromo-4-ethenylbenzene (**3g**). Using general procedure A, 4-bromobenzaldehyde (187 mg, 1.01 mmol) and HNTf₂ (1.0 mL, 1.0 mol%) provided alkene **3g** (126 mg, 0.69 mmol, 68%) as a colorless oil after purification by flash column chromatography (eluent: hexane).

R_f (hexane) = 0.49

¹H NMR (400 MHz, CDCl₃); δ 7.48–7.43 (m, 2H), 7.30–7.27 (m, 2H), 6.67 (dd, J = 17.6, 11.0 Hz, 1H), 5.78–5.73 (m, 1H), 5.29 (d, J = 11.0 Hz, 1H).

¹³C{¹H} NMR (100 MHz, CDCl₃); δ 136.6, 135.9, 131.8, 127.9, 121.7, 114.8.

Spectral data in accordance to previously published data.²²

1-Ethenyl-4-(trifluoromethyl)benzene (**3h**). Using general procedure B, 4-(trifluoromethyl)benzaldehyde (140 μL, 1.03 mmol), HNTf₂ (1.0 mL, 1.0 mol%) and 1,3,5-trimethoxybenzene (4.0 mg, 0.024 mmol) provided alkene **3h** (67% NMR yield).

¹H NMR (400 MHz, CDCl₃); δ 7.57 (d, J = 8.4 Hz, 2H), 7.49 (d, J = 8.4 Hz, 2H), 6.73 (dd, J = 17.6, 10.9 Hz, 1H), 5.84 (d, J = 17.6 Hz, 1H), 5.37 (d, J = 10.9 Hz, 1H).

4-Ethenylbenzonitrile (**3i**). Using general procedure A, 4-cyanobenzaldehyde (131 mg, 1.00 mmol) and HNTf₂ (1.0 mL, 1.0 mol%) provided alkene **3i** (90 mg, 0.75 mmol, 75%) as a colorless oil after purification by flash column chromatography (eluent: hexane:Et₂O, 4:1).

R_f (hexane) = 0.13

¹H NMR (400 MHz, CDCl₃); δ 7.62–7.50 (m, 2H), 7.49–7.47 (m, 2H), 6.73 (dd, J = 17.6, 10.9 Hz, 1H), 5.88 (d, J = 17.6 Hz, 1H), 5.45 (d, J = 10.9 Hz, 1H).

¹³C{¹H} NMR (100 MHz, CDCl₃); δ 142.0, 135.5, 132.5, 126.9, 119.1, 117.9, 111.2.

Spectral data in accordance to previously published data.²³

4-Ethenyl-1,2-dimethoxybenzene (**3j**). Using general procedure A, 3,4-dimethoxybenzaldehyde (168 mg, 1.01 mmol) and HNTf₂ (0.1 mL, 0.1 mol%) provided alkene **3j** (147 mg, 0.90 mmol, 89%) as a colorless oil after purification by flash column chromatography (eluent: hexane:Et₂O, 4:1).

R_f (hexane:Et₂O, 4:1) = 0.26

¹H NMR (400 MHz, CDCl₃); δ 6.98–6.93 (m, 2H), 6.83 (d, J = 8.2 Hz, 1H), 6.66 (dd, J = 17.5, 11.0 Hz, 1H), 5.64–5.59 (m, 1H), 5.15 (dd, J = 11.0, 0.7 Hz, 1H), 3.91 (s, 3H), 3.89 (s, 3H).

¹³C{¹H} NMR (100 MHz, CDCl₃); δ 149.10, 149.08, 136.6, 130.8, 119.6, 112.0, 111.1, 108.6, 56.1, 55.9.

Spectral data in accordance to previously published data.²⁴

3-Ethenylphenol (**3k**). Using general procedure A, 3-hydroxybenzaldehyde (123 mg, 1.01 mmol) and HNTf₂ (0.1 mL, 0.1 mol%) provided alkene **3k** (108 mg, 0.89 mmol, 88%) as a colorless oil after purification by flash column chromatography

(eluent: hexane:Et₂O, 4:1). *Note: the second step (HNTf₂ reaction) was performed in MeCN rather than 1,2-DCE due to solubility issues.*

R_f (hexane:Et₂O, 4:1) = 0.19

¹H NMR (400 MHz, CDCl₃); δ 7.21 (t, J = 7.9 Hz, 1H), 7.01–6.98 (m, 1H), 6.91–6.90 (m, 1H), 6.76–6.73 (m, 1H), 6.67 (dd, J = 17.4, 11.0 Hz, 1H), 5.73 (d, J = 17.4 Hz, 1H), 5.26 (d, J = 11.0 Hz, 1H), 5.06 (s, 1H).

¹³C{¹H} NMR (100 MHz, CDCl₃); δ 155.8, 139.4, 136.6, 129.9, 119.3, 115.0, 114.5, 112.9.

Spectral data in accordance to previously published data.²⁵

2-Ethenylnaphthalene (**3l**). Using general procedure A, 2-naphthaldehyde (157 mg, 1.01 mmol) and HNTf₂ (0.1 mL, 0.1 mol%) provided alkene **3l** (129 mg, 0.84 mmol, 83%) as a white solid after purification by flash column chromatography (eluent: hexane).

R_f (hexane) = 0.42

¹H NMR (400 MHz, CDCl₃); δ 7.86–7.81 (m, 4H), 7.78 (s, 1H), 7.67 (dd, J = 8.6, 1.6 Hz, 1H), 7.51–7.44 (m, 2H), 6.91 (dd, J = 17.6, 10.9 Hz, 1H), 5.90 (d, J = 17.6 Hz, 1H), 5.37 (d, J = 10.9 Hz, 1H).

¹³C{¹H} NMR (100 MHz, CDCl₃); δ 137.1, 135.1, 133.7, 133.3, 128.3, 128.2, 127.8, 126.5, 126.4, 126.0, 123.3, 114.3.

Spectral data in accordance to previously published data.²²

2-Ethenylthiophene (**3m**). Using general procedure B, 2-thiophenecarboxaldehyde (93 μL, 1.00 mmol), HNTf₂ (0.1 mL, 0.1 mol%) and 1,3,5-trimethoxybenzene (3.3 mg, 0.020 mmol) provided alkene **3m** (60% NMR yield).

2-Ethenylfuran (**3n**). Using general procedure B, furfural (83 μL, 1.00 mmol), HNTf₂ (0.1 mL, 0.1 mol%) and 1,3,5-trimethoxybenzene (3.0 mg, 0.018 mmol) provided alkene **3n** (75% NMR yield).

¹H NMR (400 MHz, CDCl₃); δ 7.37–7.33 (m, 1H), 6.51 (dd, J = 17.6, 11.3 Hz, 1H), 6.37 (dd, J = 3.3, 1.8 Hz, 1H), 6.26 (d, J = 3.3 Hz, 1H), 5.66 (dd, J = 17.6, 1.2 Hz, 1H), 5.16 (dd, J = 11.3, 1.2 Hz, 1H).

Ethenylcyclohexane (**3o**). Using general procedure B, cyclohexanecarboxaldehyde (120 μL, 0.99 mmol), HNTf₂ (0.5 mL, 0.5 mol%) and 1,3,5-trimethoxybenzene (3.1 mg, 0.018 mmol) provided alkene **3o** (64% NMR yield).

tert-Butyl 4-methylidenepiperidine-1-carboxylate (**3p**). Using general procedure A, *N*-Boc-4-piperidone (298 mg, 1.50 mmol) and HNTf₂ (0.1 mL, 0.1 mol%) provided alkene **3p** (117 mg, 0.59 mmol, 40%) as a colorless oil after purification by flash column chromatography (eluent: hexane:EtOAc, 14:1).

R_f (hexane:EtOAc, 2:1) = 0.61

¹H NMR (400 MHz, CDCl₃); δ 4.74 (s, 2H), 3.43–3.39 (m, 4H), 2.19–2.16 (m, 4H), 1.46 (s, 9H).

¹³C{¹H} NMR (100 MHz, CDCl₃); δ 154.9, 145.6, 109.2, 79.7, 45.5, 34.7, 28.6.

Spectral data in accordance to previously published data.²⁶

4-Methylideneoxane (**3q**). Using general procedure B, 4-oxotetrahydropyran (92 μL, 1.00 mmol), HNTf₂ (1.0 mL, 1.0 mol%) and 1,3,5-trimethoxybenzene (3.8 mg, 0.023 mmol) provided alkene **3q** (64% NMR yield).

Trimethyl(3-phenylbut-3-en-1-yn-1-yl)silane (5a). Using general procedure A, ketone **4a** (67 mg, 0.33 mmol) and HNTf₂ (33 μ L, 0.1 mol%) provided enyne **5a** (47 mg, 0.24 mmol, 72%) as a pale yellow oil after purification by flash column chromatography (eluent: hexane). *Note: crude and isolated samples of enynes 5 degraded regardless of storage temperature (See supporting information).*

R_f (hexane-EtOAc, 2:1) = 0.63

¹H NMR (400 MHz, CDCl₃); δ 7.66–7.63 (m, 2H), 7.38–7.31 (m, 3H), 5.94 (d, J = 0.8 Hz, 1H), 5.71 (s, 1H), 0.26 (s, 9H).

¹³C{¹H} NMR (100 MHz, CDCl₃); δ 137.0, 130.7, 128.50, 128.45, 126.2, 121.6, 104.2, 96.0, 0.09.

Spectral data in accordance to previously published data.²⁷

Trimethyl[3-(naphthalen-2-yl)but-3-en-1-yn-1-yl]silane (5b). Using general procedure B, ketone **4b** (93 mg, 0.37 mmol), HNTf₂ (37 μ L, 0.1 mol%) and 1,3,5-trimethoxybenzene (3.8 mg, 0.023 mmol) provided enyne **5b** (87% NMR yield).

[3-(4-bromophenyl)but-3-en-1-yn-1-yl](trimethyl)silane (5c). Using general procedure B, ketone **4c** (142 mg, 0.51 mmol), HNTf₂ (50 μ L, 0.1 mol%) and 1,3,5-trimethoxybenzene (3.9 mg, 0.023 mmol) provided enyne **5c** (86% NMR yield).

¹H NMR (400 MHz, CDCl₃); δ 7.51–7.44 (m, 4H), 5.91–5.89 (m, 1H), 5.71–5.70 (m, 1H), 0.24 (s, 9H).

Trimethyl[3-(thiophen-2-yl)but-3-en-1-yn-1-yl]silane (5d). Using general procedure B, ketone **4d** (104 mg, 0.50 mmol), HNTf₂ (50 μ L, 0.1 mol%) and 1,3,5-trimethoxybenzene (2.1 mg, 0.013 mmol) provided enyne **5d** (51% NMR yield). ASSOCIATED CONTENT

Supporting Information

Copies of spectra and exemplar yield calculation.

AUTHOR INFORMATION

Corresponding Author

*E-mail: m.mclaughlin@mmu.ac.uk

Notes

The authors declare no competing financial interests.

ACKNOWLEDGMENT

We thank Manchester Metropolitan University (MMU) for startup funding. TKB thanks MMU for a strategic opportunities fund award. MML thanks MMU, Royal Society of Chemistry and Medical Research Council for funding. We also thank Kate Jones for synthetic assistance.

REFERENCES

- (a) Peterson, D. J., *Carbonyl olefination reaction using silyl-substituted organometallic compounds*. *J. Org. Chem.* **1968**, *33*, 780; (b) Staden, L. F. v.; Gravestock, D.; Ager, D. J., *New developments in the Peterson olefination reaction*. *Chem. Soc. Rev.* **2002**, *31*, 195.
- (a) Takeda, T., *Modern Carbonyl Olefination: Methods and Applications*. Wiley-VCH2014; (b) Wender, P. A.; Hegde, S. G.; Hubbard, R. D.; Zhang, L., *Total Synthesis of (–)-Laulimalide*. *J. Am. Chem. Soc.* **2002**, *124*, 4956; (c) Stathakis, C. I.; Yioti, E. G.; Gallos, J. K., *Total Syntheses of (–)- α -Kainic Acid*. *Eur. J. Org. Chem.* **2012**, *2012*, 4661.
- Lambert, J. B.; Wang, G. T.; Finzel, R. B.; Teramura, D. H., *Stabilization of positive charge by β -silicon*. *J. Am. Chem. Soc.* **1987**, *109*, 7838.
- Das, M.; O'Shea, D. F., *Z-Stereoselective Aza-Peterson Olefinations with Bis(trimethylsilane) Reagents and Sulfinyl Imines*. *Org. Lett.* **2016**, *18*, 336.
- (a) Hamlin, T. A.; Kelly, C. B.; Cywar, R. M.; Leadbeater, N. E., *Methylenation of Perfluoroalkyl Ketones using a Peterson Olefination Approach*. *J. Org. Chem.* **2014**, *79*, 1145; (b) Hamlin, T. A.; Lazarus, G. M. L.; Kelly, C. B.; Leadbeater, N. E., *A Continuous-Flow Approach to 3,3,3-Trifluoromethylpropenes: Bringing Together Grignard Addition, Peterson Elimination, Inline Extraction, and Solvent Switching*. *Org. Process Res. Dev.* **2014**, *18*, 1253; (c) Wang, Y.; Du, G.-F.; Gu, C.-Z.; Xing, F.; Dai, B.; He, L., *N-heterocyclic carbene-catalysed Peterson olefination reaction*. *Tetrahedron* **2016**, *72*, 472; (d) Manvar, A.; O'Shea, D. F., *Trimethylsilyloxy-Catalysed Peterson Olefinations with 2,2-Bis(trimethylsilyl)-1,3-dithiane*. *European Journal of Organic Chemistry* **2015**, *2015*, 7259.
- Reuping, M.; Parmer, D.; Sugiono, E., *Asymmetric Brønsted Acid Catalysis*. Wiley-VCH2015.
- (a) Merad, J.; Lalli, C.; Bernadat, G.; Maury, J.; Masson, G., *Enantioselective Brønsted Acid Catalysis as a Tool for the Synthesis of Natural Products and Pharmaceuticals*. *Chemistry – A European Journal* **2018**, *24*, 3925; (b) Uraguchi, D.; Terada, M., *Chiral Brønsted Acid-Catalyzed Direct Mannich Reactions via Electrophilic Activation*. *J. Am. Chem. Soc.* **2004**, *126*, 5356.

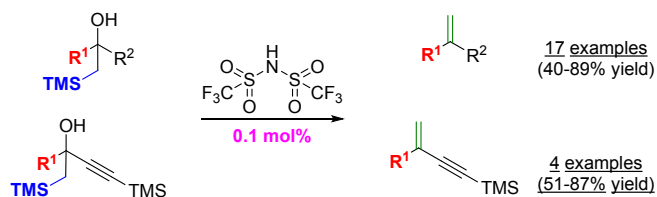
8. Taylor, M. S.; Jacobsen, E. N., *Asymmetric Catalysis by Chiral Hydrogen-Bond Donors*. *Angew. Chem. Int. Ed.* **2006**, *45*, 1520.
9. Madarász, Á.; Dósa, Z.; Varga, S.; Soós, T.; Csámpai, A.; Pápai, I., *Thiourea Derivatives as Brønsted Acid Organocatalysts*. *ACS Catalysis* **2016**, *6*, 4379.
10. Yamamoto, H.; Ishihara, K., *Acid Catalysis in Modern Organic Synthesis*. Wiley-VCH2008.
11. (a) Orizu, I.; Bolshan, Y., *A general Brønsted acid-catalyzed allylation of benzhydryl alcohols*. *Tetrahedron Lett.* **2016**, *57*, 5798; (b) Stanek, F.; Stodulski, M., *Organocatalytic α -Allylation of α -Branched Aldehydes by Synergistic Catalysis of Brønsted Acids and Amines*. *Eur. J. Org. Chem.* **2016**, 2016, 4768; (c) Sanz, R.; Martínez, A.; Álvarez-Gutiérrez, J. M.; Rodríguez, F., *Metal-Free Catalytic Nucleophilic Substitution of Propargylic Alcohols*. *Eur. J. Org. Chem.* **2006**, 2006, 1383; (d) Sanz, R.; Martínez, A.; Miguel, D.; Álvarez-Gutiérrez, J. M.; Rodríguez, F., *Brønsted Acid-Catalyzed Nucleophilic Substitution of Alcohols*. *Adv. Synth. Catal.* **2006**, 348, 1841.
12. (a) Akiyama, T.; Mori, K., *Stronger Brønsted Acids: Recent Progress*. *Chem. Rev.* **2015**, *115*, 9277; (b) Cheon, C. H.; Yamamoto, H., *Super Brønsted acid catalysis*. *Chem. Commun. (Camb.)* **2011**, 47, 3043.
13. Zhao, W.; Sun, J., *Triflimide (HNTf₂) in Organic Synthesis*. *Chem. Rev.* **2018**, *118*, 10349.
14. Raamat, E.; Kaupmees, K.; Ovsjannikov, G.; Trummel, A.; Kütt, A.; Saame, J.; Koppel, I.; Kaljurand, I.; Lipping, L.; Rodima, T.; Pihl, V.; Koppel, I. A.; Leito, I., *Acidities of strong neutral Brønsted acids in different media*. *J. Phys. Org. Chem.* **2013**, *26*, 162.
15. Denmark, S. E.; Yang, S.-M., *Total Synthesis of (+)-Brasilenyne. Application of an Intramolecular Silicon-Assisted Cross-Coupling Reaction*. *J. Am. Chem. Soc.* **2004**, *126*, 12432.
16. Lambert, J. B.; Kania, L.; Schilf, W.; McConnell, J. A., *Trimethylsilyl and related cations in solution*. *Organometallics* **1991**, *10*, 2578.
17. (a) Shu, X.-Z.; Li, X.; Shu, D.; Huang, S.; Schienebeck, C. M.; Zhou, X.; Robichaux, P. J.; Tang, W., *Rhodium-Catalyzed Intra- and Intermolecular [5 + 2] Cycloaddition of 3-Acyloxy-1,4-enyne and Alkyne with Concomitant 1,2-Acyloxy Migration*. *J. Am. Chem. Soc.* **2012**, *134*, 5211; (b) Xu, W.; Chen, M.; Sun, N.; Liu, Y., *Gold-catalyzed cyclization of 1,6-diynyl dithioacetals via 1,7-carbene transfer and aromatic C–H functionalization*. *Chem. Commun.* **2016**, 52, 11000; (c) Wendlandt, A. E.; Vangal, P.; Jacobsen, E. N., *Quaternary stereocentres via an enantioconvergent catalytic S_N1 reaction*. *Nature* **2018**, *556*, 447; (d) Shi Shun, A. L. K.; Chernick, E. T.; Eisler, S.; Tykwinski, R. R., *Synthesis of Unsymmetrically Substituted 1,3-Butadiynes and 1,3,5-Hexatriynes via Alkylidene Carbenoid Rearrangements*. *J. Org. Chem.* **2003**, *68*, 1339.
18. Xu, S.; Gao, Y.; Chen, R.; Wang, K.; Zhang, Y.; Wang, J., *Copper(i)-catalyzed olefination of N-sulfonylhydrazones with sulfones*. *Chem. Commun.* **2016**, 52, 4478.
19. Tang, J.; Hackenberger, D.; Goossen, L. J., *Branched Arylalkenes from Cinnamates: Selectivity Inversion in Heck Reactions by Carboxylates as Deciduous Directing Groups*. *Angew. Chem. Int. Ed.* **2016**, *55*, 11296.
20. Lei, C.; Yip, Y. J.; Zhou, J. S., *Nickel-Catalyzed Direct Synthesis of Aryl Olefins from Ketones and Organoboron Reagents under Neutral Conditions*. *J. Am. Chem. Soc.* **2017**, *139*, 6086.
21. Chatalova-Sazepin, C.; Wang, Q.; Sammis, G. M.; Zhu, J., *Copper-Catalyzed Intermolecular Carboetherification of Unactivated Alkenes by Alkyl Nitriles and Alcohols*. *Angew. Chem. Int. Ed.* **2015**, *54*, 5443.

22. Chen, W.; Tao, H.; Huang, W.; Wang, G.; Li, S.; Cheng, X.; Li, G., *Hantzsch Ester as a Photosensitizer for the Visible-Light-Induced Debromination of Vicinal Dibromo Compounds*. *Chemistry – A European Journal* **2016**, 22, 9546.
23. Zhang, J.-z.; Tang, Y., *Iron-Catalyzed Regioselective Oxo- and Hydroxy-Phthalimide of Styrenes: Access to α -Hydroxyphthalimide Ketones*. *Adv. Synth. Catal.* **2016**, 358, 752.
24. Siddiki, S. M. A. H.; Touchy, A. S.; Kon, K.; Shimizu, K.-i., *Direct Olefination of Alcohols with Sulfones by Using Heterogeneous Platinum Catalysts*. *Chemistry – A European Journal* **2016**, 22, 6111.
25. Wienhöfer, G.; Westerhaus, F. A.; Jagadeesh, R. V.; Junge, K.; Junge, H.; Beller, M., *Selective iron-catalyzed transfer hydrogenation of terminal alkynes*. *Chem. Commun.* **2012**, 48, 4827.
26. Green, S. A.; Vásquez-Céspedes, S.; Shenvi, R. A., *Iron–Nickel Dual-*

Catalysis: A New Engine for Olefin Functionalization and the Formation of Quaternary Centers. *J. Am. Chem. Soc.* **2018**, 140, 11317.

27. Yan, W.; Ye, X.; Akhmedov, N. G.; Petersen, J. L.; Shi, X., *1,2,3-Triazole: Unique Ligand in Promoting Iron-Catalyzed Propargyl Alcohol Dehydration*. *Org. Lett.* **2012**, 14, 2358.

TOC Graphic



1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
